

CLAIMS

1. A method for detecting or selecting a dopaminergic neuron and/or a progenitor cell thereof, wherein the method comprises the step of contacting a cellular sample potentially
5 comprising a dopaminergic neuron and/or a progenitor cell thereof with a polynucleotide that hybridizes under stringent conditions to a transcript of a gene that consists of a nucleotide sequence of any one of (1) to (6):

(1) the nucleotide sequence of SEQ ID NO: 13;

(2) a nucleotide sequence encoding a polypeptide consisting of the amino acid sequence of SEQ
10 ID NO: 14;

(3) a nucleotide sequence that hybridizes under stringent conditions to a gene consisting of the nucleotide sequence of SEQ ID NO: 13;

(4) the nucleotide sequence of SEQ ID NO: 15 or 17;

(5) a nucleotide sequence encoding a polypeptide consisting of the amino acid sequence of SEQ
15 ID NO: 16 or 18; and

(6) a nucleotide sequence that hybridizes under stringent conditions to a gene consisting of the nucleotide sequence of SEQ ID NO: 15 or 17.

2. The method of claim 1, wherein the polynucleotide comprises at least 15 nucleotides.
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3. A reagent for distinguishing a dopaminergic neuron and/or a progenitor cell thereof, wherein the reagent comprises, as an active ingredient, a polynucleotide that hybridizes under
stringent conditions to a transcript of a gene that consists of a nucleotide sequence of any one of
(1) to (6):

25 (1) the nucleotide sequence of SEQ ID NO: 13;

(2) a nucleotide sequence encoding a polypeptide consisting of the amino acid sequence of SEQ
ID NO: 14;

(3) a nucleotide sequence that hybridizes under stringent conditions to a gene consisting of the nucleotide sequence of SEQ ID NO: 13;

30 (4) the nucleotide sequence of SEQ ID NO: 15 or 17;

(5) a nucleotide sequence encoding a polypeptide consisting of the amino acid sequence of SEQ
ID NO: 16 or 18; and

(6) a nucleotide sequence that hybridizes under stringent conditions to a gene consisting of the nucleotide sequence of SEQ ID NO: 15 or 17.
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4. The reagent of claim 3, wherein the polynucleotide comprises at least 15 nucleotides.

5. A method for detecting or selecting a dopaminergic neuron and/or a progenitor cell thereof, wherein the method comprises the step of contacting a cellular sample potentially comprising a dopaminergic neuron and/or a progenitor cell thereof with an antibody that binds to a polypeptide that consists of an amino acid sequence of any one of (1) to (6) or a partial sequence thereof:

(1) the amino acid sequence of SEQ ID NO: 14;

(2) an amino acid sequence with a deletion, insertion, substitution, or addition of one or more amino acids in the amino acid sequence of SEQ ID NO: 14;

(3) an amino acid sequence encoded by a nucleotide sequence that hybridizes under stringent conditions to a gene consisting of the nucleotide sequence of SEQ ID NO: 13;

(4) the amino acid sequence of SEQ ID NO: 16 or 18;

(5) an amino acid sequence with a deletion, insertion, substitution, or addition of one or more amino acids in the amino acid sequence of SEQ ID NO: 16 or 18; and

(6) an amino acid sequence encoded by a nucleotide sequence that hybridizes under stringent conditions to a gene consisting of the nucleotide sequence of SEQ ID NO: 15 or 17.

6. The method of claim 5, wherein the polypeptide consisting of a partial sequence comprises at least six consecutive amino acid residues.

7. A reagent for distinguishing a dopaminergic neuron and/or a progenitor cell thereof wherein the reagent comprises, as an active ingredient, an antibody that binds to a polypeptide that consists of an amino acid sequence of any one of (1) to (6) or a partial sequence thereof:

(1) the amino acid sequence of SEQ ID NO: 14;

(2) an amino acid sequence with a deletion, insertion, substitution, or addition of one or more amino acids in the amino acid sequence of SEQ ID NO: 14;

(3) an amino acid sequence encoded by a nucleotide sequence that hybridizes under stringent conditions to a gene consisting of the nucleotide sequence of SEQ ID NO: 13;

(4) the amino acid sequence of SEQ ID NO: 16 or 18;

(5) an amino acid sequence with a deletion, insertion, substitution, or addition of one or more amino acids in the amino acid sequence of SEQ ID NO: 16 or 18; and

(6) an amino acid sequence encoded by a nucleotide sequence that hybridizes under stringent conditions to a gene consisting of the nucleotide sequence of SEQ ID NO: 15 or 17.

8. The reagent of claim 7, wherein the polypeptide consisting of a partial sequence comprises at least six consecutive amino acid residues.

9. A method for detecting or selecting a dopaminergic neuron and/or a progenitor cell thereof, wherein the method comprises the steps of:

(a) contacting a cellular sample potentially comprising a dopaminergic neuron and/or a progenitor cell thereof with a polynucleotide that hybridizes under stringent conditions to a transcript of a gene that consists of a nucleotide sequence from any one of (a-1) to (a-6):

(a-1) the nucleotide sequence of SEQ ID NO: 13;

(a-2) a nucleotide sequence encoding a polypeptide consisting of the amino acid sequence of SEQ ID NO: 14;

(a-3) a nucleotide sequence that hybridizes under stringent conditions to a gene consisting of the nucleotide sequence of SEQ ID NO: 13;

(a-4) the nucleotide sequence of SEQ ID NO: 15 or 17;

(a-5) the nucleotide sequence encoding a polypeptide consisting of the amino acid sequence of SEQ ID NO: 16 or 18; and

(a-6) a nucleotide sequence that hybridizes under stringent conditions to a gene consisting of the nucleotide sequence of SEQ ID NO: 15 or 17; and

(b) contacting a cellular sample potentially comprising a dopaminergic neuron and/or a progenitor cell thereof with a polynucleotide that hybridizes under stringent conditions to transcripts of one or more genes selected from the group consisting of Lmx1b, Nurr1, En1, Ptx3, and TH, or with an antibody that binds to translation products of said selected genes.

10. The method of claim 9, which further comprises the step of:

(c) contacting a cellular sample potentially comprising the dopaminergic neuron and/or the progenitor cell thereof with a polynucleotide that hybridizes under stringent conditions to transcripts of either or both of the genes selected from DAT and ADH2 or with an antibody that binds to a translation product of a said selected gene.

11. The method of claim 9, wherein the gene selected in step (b) is one or more of Lmx1b, Nurr1, or En1.

12. A method for detecting or selecting a dopaminergic neuron and/or a progenitor cell thereof, wherein the method comprises the steps of:

(a) contacting a cellular sample potentially comprising a dopaminergic neuron and/or a progenitor cell thereof with a polynucleotide that hybridizes under stringent conditions to a transcript of a gene that consists of a nucleotide sequence from any one of (a-1) to (a-6):

(a-1) the nucleotide sequence of SEQ ID NO: 13;

(a-2) a nucleotide sequence encoding a polypeptide consisting of the amino acid sequence of SEQ ID NO: 14;

(a-3) a nucleotide sequence that hybridizes under stringent conditions to a gene consisting of the nucleotide sequence of SEQ ID NO: 13;

5 (a-4) the nucleotide sequence of SEQ ID NO: 15 or 17;

(a-5) a nucleotide sequence encoding a polypeptide consisting of the amino acid sequence (human) of SEQ ID NO: 16 or 18; and

(a-6) a nucleotide sequence that hybridizes under stringent conditions to a gene consisting of the nucleotide sequence of SEQ ID NO: 15 or 17; and

10 (b) contacting a cellular sample potentially comprising a dopaminergic neuron and/or a progenitor cell thereof with a polynucleotide that hybridizes under stringent conditions to transcripts of either or both of the genes selected from DAT and ADH2, or with an antibody that binds to translation products of said selected genes.

15 13. The method of any one of claims 9 to 12, wherein the polynucleotide is a nucleotide sequence comprising at least 15 consecutive nucleotides.

14. A kit for distinguishing a dopaminergic neuron and/or a progenitor cell thereof, wherein the kit comprises: the reagent of claim 3 or 4; and a polynucleotide that hybridizes under
20 stringent conditions to transcripts of one or more genes selected from the group consisting of Lmx1b, Nurr1, En1, Ptx3, TH, DAT, and ADH2.

15. A kit for distinguishing a dopaminergic neuron and/or a progenitor cell thereof, wherein the kit comprises: the reagent of claim 3 or 4; and an antibody that binds to translation products
25 of one or more genes selected from the group consisting of Lmx1b, Nurr1, En1, Ptx3, TH, DAT, and ADH2.

16. A method for detecting or selecting a dopaminergic neuron and/or a progenitor cell thereof, wherein the method comprises the steps of:

30 (a) contacting a cellular sample potentially comprising a dopaminergic neuron and/or a progenitor cell thereof with an antibody that binds to a polypeptide consisting of an amino acid sequence of any one of (a-1) to (a-6) or a partial sequence thereof:

(a-1) the amino acid sequence of SEQ ID NO: 14;

(a-2) an amino acid sequence with a deletion, insertion, substitution, or addition of one
35 or more amino acids in the amino acid sequence of SEQ ID NO: 14;

(a-3) an amino acid sequence encoded by a nucleotide sequence that hybridizes under

stringent conditions to a gene consisting of the nucleotide sequence of SEQ ID NO: 13;

(a-4) the amino acid sequence of SEQ ID NO: 16 or 18;

(a-5) an amino acid sequence with a deletion, insertion, substitution, or addition of one or more amino acids in the amino acid sequence of SEQ ID NO: 16 or 18; and

(a-6) an amino acid sequence encoded by a nucleotide sequence that hybridizes under stringent conditions to a gene consisting of the nucleotide sequence of SEQ ID NO: 15 or 17; and

(b) contacting a cellular sample potentially comprising a dopaminergic neuron and/or a progenitor cell thereof with a polynucleotide that hybridizes under stringent conditions to transcripts of one or more genes selected from the group consisting of Lmx1b, Nurr1, En1, Ptx3, and TH, or with an antibody that binds to translation products of said selected genes.

17. The method of claim 16, which further comprises the step of:

(c) contacting a cellular sample potentially comprising a dopaminergic neuron and/or a progenitor cell thereof with a polynucleotide that hybridizes under stringent conditions to transcripts of either or both of the genes selected from DAT and ADH2 or with an antibody that binds to translation products of said selected genes.

18. The method of claim 16, wherein the genes selected in step (b) is one or more of Lmx1b, Nurr1, or En1.

19. A method for detecting or selecting a dopaminergic neuron and/or a progenitor cell thereof, wherein the method comprises the steps of:

(a) contacting a cellular sample potentially comprising a dopaminergic neuron and/or a progenitor cell thereof with an antibody that binds to a polypeptide consisting of an amino acid sequence of any one of (a-1) to (a-6) or a partial sequence thereof:

(a-1) the amino acid sequence of SEQ ID NO: 14;

(a-2) an amino acid sequence with a deletion, insertion, substitution, or addition of one or more amino acids in the amino acid sequence of SEQ ID NO: 14;

(a-3) an amino acid sequence encoded by a nucleotide sequence that hybridizes under stringent conditions to a gene consisting of the nucleotide sequence of SEQ ID NO: 13;

(a-4) the amino acid sequence of SEQ ID NO: 16 or 18;

(a-5) an amino acid sequence with a deletion, insertion, substitution, or addition of one or more amino acids in the amino acid sequence of SEQ ID NO: 16 or 18; and

(a-6) an amino acid sequence encoded by a nucleotide sequence that hybridizes under stringent conditions to a gene consisting of the nucleotide sequence of SEQ ID NO: 15 or 17;

and

(b) contacting a cellular sample potentially comprising a dopaminergic neuron and/or a progenitor cell thereof with a polynucleotide that hybridizes under stringent conditions to transcripts of either or both of the genes selected from DAT and ADH2, or with an antibody that binds to translation products of said selected genes.

20. The method of any one of claims 16 to 19, wherein the polypeptide consisting of a partial sequence comprises at least 6 consecutive amino acid residues.

21. A kit for distinguishing a dopaminergic neuron and/or progenitor cell thereof, wherein the kit comprises: the reagent of claim 7 or 8; and a polynucleotide that hybridizes under stringent conditions to transcripts of one or more genes selected from the group consisting of Lmx1b, Nurr1, En1, Ptx3, TH, DAT, and ADH2.

22. A kit for distinguishing a dopaminergic neuron and/or a progenitor cell thereof, wherein the kit comprises: the reagent of claim 7 or 8; and an antibody that binds to translation products of one or more genes selected from the group consisting of Lmx1b, Nurr1, En1, Ptx3, TH, DAT, and ADH2.

23. A method of screening for a differentiation-inducing reagent for a dopaminergic neuron, wherein the method comprises the steps of:

(a) contacting a test substance with cells that can be differentiated into dopaminergic neurons;
 (b) detecting a transcript of the Lmx1a gene by contacting the cells, after contact with the test substance, with a polynucleotide that hybridizes under stringent conditions to a transcript of a gene consisting of a nucleotide sequence of any one of (b-1) to (b-6):

(b-1) the nucleotide sequence of SEQ ID NO: 13;

(b-2) a nucleotide sequence encoding a polypeptide consisting of the amino acid sequence of SEQ ID NO: 14;

(b-3) a nucleotide sequence that hybridizes under stringent conditions to a gene consisting of the nucleotide sequence of SEQ ID NO: 13;

(b-4) the nucleotide sequence of SEQ ID NO: 15 or 17;

(b-5) the nucleotide sequence encoding a polypeptide consisting of the amino acid sequence of SEQ ID NO: 16 or 18; and

(b-6) a nucleotide sequence that hybridizes under stringent conditions to a gene consisting of the nucleotide sequence of SEQ ID NO: 15 or 17; and

(c) determining whether the test substance can induce the differentiation of dopaminergic

neurons when the transcript of the *Lmx1a* gene is detected.

24. The method of claim 23, wherein the polynucleotide is a nucleotide sequence comprising at least 15 consecutive nucleotides.

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25. A method of screening for a differentiation-inducing reagent for a dopaminergic neuron, wherein the method comprises the steps of:

(a) contacting a test substance with cells that can be differentiated into dopaminergic neurons;
 (b) detecting a translation product of the *Lmx1a* gene by contacting the cells, after contact with
 10 the test substance, with an antibody that binds to a polypeptide consisting of an amino acid sequence of any one of (b-1) to (b-6) or a partial sequence thereof:

(b-1) the amino acid sequence of SEQ ID NO: 14;

(b-2) an amino acid sequence with a deletion, insertion, substitution, or addition of one or more amino acids in the amino acid sequence of SEQ ID NO: 14;

15 (b-3) an amino acid sequence encoded by a nucleotide sequence that hybridizes under stringent conditions to a gene consisting of the nucleotide sequence of SEQ ID NO: 13;

(b-4) the amino acid sequence of SEQ ID NO: 16 or 18;

(b-5) an amino acid sequence with a deletion, insertion, substitution, or addition of one or more amino acids in the amino acid sequence of SEQ ID NO: 16 or 18; and

20 (b-6) an amino acid sequence encoded by a nucleotide sequence that hybridizes under stringent conditions to a gene consisting of the nucleotide sequence of SEQ ID NO: 15 or 17; and

(c) determining whether the test substance can induce the differentiation of dopaminergic neurons when the translation product of the *Lmx1a* gene is detected.

25 26. The method of claim 25, wherein the polypeptide consisting of a partial sequence comprises at least six consecutive amino acid residues.